

REMARKS

Claims 11, 13-15, 17-26, and 71-80 are pending in the subject U.S. patent application and have been examined. Claims 1-80 as filed were subjected to a Restriction/Election Requirement. In response to the Restriction/Election Requirement, applicants elected claims 11-26 and 71-80 for prosecution. Claims 1-10 and 27-70 have been canceled herein without prejudice as being drawn to unelected subject matter.

The United States Patent and Trademark Office (hereinafter the "Patent Office") has objected to the specification upon the assertion that the abstract of the disclosure is not descriptive of the claimed subject matter and is not in proper English, based on the contention that the present abstract is a sentence fragment.

The Patent Office has objected to the specification upon the contention that the disclosure contains an embedded hyperlink on page 58, line 7. Applicants have amended the specification to remove this hyperlink in accordance with a suggestion from the Examiner. A marked up copy of the paragraph containing the objected to text is provided hereinabove.

Claims 11, 13-15, 17-26, and 71-80 have been rejected under 35 U.S.C. § 101 upon the contention that the claimed invention is not supported by either a substantial asserted utility or a well-established utility.

Claims 11, 13-15, 17-26, and 71-80 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that since the claimed invention is not supported by either a substantial utility or a well established utility, one of skill in the art would not know how to make and use the claimed invention.

Claims 11, 13-15, 17-26, and 71-80 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed.

The specification has been amended. New claim 81 has been added. Support for the amendments can be found throughout the specification as filed,

including in Sequence Listing and in the claims. No new matter has been introduced as a result of the amendments to the specification or to the claims.

Response to the Objection to the Abstract

The Patent Office has objected to the specification upon the assertion that the abstract of the disclosure is not descriptive of the claimed subject matter and is not in proper English – the present abstract asserted to be a sentence fragment. In accordance with the suggestion of the Examiner, applicants respectfully request that this objection be held in abeyance until such time as one or more claims are in condition for allowance.

Response to the Objection to the Specification

The Patent Office has objected to the specification upon the contention that the disclosure contains an embedded hyperlink on page 58, line 7. Applicants have amended the specification to remove this hyperlink by deleting the "http:www" portion of the noted hyperlink in the marked up copy of the paragraph containing the objected to text provided hereinabove. Accordingly, applicants respectfully request that the objection to the specification be withdrawn.

Response to the Claim Rejection under 35 U.S.C. § 101

Claims 11, 13-15, 17-26 and 71-80 have been rejected upon the contention that the claimed invention is not supported by either a substantial asserted utility or a well-established utility. According to the Patent Office, SEQ ID NO: 13 comprises undefined nucleotides, and "hence it would require additional experimentation to isolate the complete coding sequence and to conform the function of the claimed isolated nucleic acids as claimed". Official Action at page 5.

After careful consideration of the rejection and the Patent Office's bases therefor, applicants respectfully traverse the rejection and submit the following.

Initially, the Patent Office's attention is directed to Public Comment (19) concerning the Utility Guidelines and the Patent Office's response thereto, published in Volume 66 of the Federal Register on page 1096, and concerning homology-based assertions of utility. The Patent Office's response indicated that a fact dependent inquiry is required because "the commenters provide no scientific evidence that homology-based assertions of utility are inherently unbelievable or involve implausible scientific principles". 66 Federal Register at page 1096, citing *In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995).

According to the Utility Examination Guidelines printed in the Federal Register,

a patent examiner must accept a utility asserted by an applicant unless the Office has evidence or sound scientific reasoning to rebut the assertion. The examiner's decision must be supported by a preponderance of the evidence... More specifically, when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient... The Office will take into account both the nature and the degree of the homology.

Utility Examination Guidelines at page 1096 (citations omitted and emphasis added). Applicants respectfully submit that the Patent Office has not provided evidence or sound scientific reasoning to rebut the assertion in the present specification that currently claimed nucleic acids encode functional polypeptides, nor is the Patent Office's decision supported by a preponderance of the evidence.

Applicants respectfully submit that the instant claims are directed, *inter alia*, to isolated and purified nucleic acid molecules encoding a soybean *rhg1* and SDS resistance gene. See Figure 3 of the subject U.S. patent application as filed. The gene is capable of conveying *Heterodera glycines*-infestation resistance or *Fusarium solani*-infection resistance to a non-resistant soybean germplasm, the gene located within a quantitative trait locus mapping to linkage

group G and mapped by genetic markers of SEQ ID NOs:1-6, said gene located along said quantitative trait locus between said markers. Positional cloning methods were used to isolate genomic sequences in the chromosomal regions of Forrest that confers SCN/SDS resistance, as further described in Example 4 in the subject U.S. patent application as filed. Specifically, *rhg1* sequences were derived from BAC clones 21D9 and 73P6 of the Forrest *Bam*HI or *Hind*III BAC libraries. In some embodiments, the gene comprises the nucleotide sequence set forth as SEQ ID NO:13 (Figure 7A-7B of the subject U.S. patent application as filed). BLASTP analysis of the translation of the *rhg1* gene (Figure 7C of the subject U.S. patent application as filed), set forth as SEQ ID:14 shows high homology to the T46070 GenBank entry described as hypothetical protein T18N14.120 from *Arabidopsis thaliana* (Figure 7E-7F of the subject U.S. patent application as filed), homology to the rice Xa21 disease resistance gene encoding a leucine-rich repeat protein, and homology to the tomato CF-2 gene for resistance to *Cladosporium fulvus* (Figure 7D of the subject U.S. patent application as filed).

Applicants respectfully submit that the instant claims are directed, *inter alia*, to isolated and purified nucleic acid molecules encoding a soybean *Rhg4* gene. The gene is capable of conveying *Heterodera glycines*-infestation resistance to a non-resistant soybean germplasm, the gene located within a quantitative trait locus mapping to linkage group A2 and mapped by the AFLP markers of SEQ ID NOs:6-12, the gene located along said quantitative trait locus between said markers. Preferably, the gene comprises a nucleotide sequence set forth as any one of SEQ ID NOs:16-19. Genes underlying quantitative traits, or genes with related function, such as disease resistance, are often organized in clusters within the genome (e.g., Staskawicz (1995) *Science* 268:661-667). In the case of SCN/SDS resistance, previous studies by the co-inventors of the presently disclosed subject matter have suggested that the resistance trait in Forrest may be caused by four genes in a cluster with two pairs in close linkage or by a two-gene cluster with each gene displaying pleiotropy (Meksem et al., 1999). Thus, genomic DNA isolated and disclosed herein comprise multiple

resistance gene sequences. Additional sequences derived from the SCN/SDS resistance locus are set forth as SEQ ID NOs:20-66. BLASTX analysis of these sequences reveals further homology to known proteins in other organisms. Of particular interest, BLASTX analysis of the sequences set forth as SEQ ID NOs:67-114 reveals that several of the disclosed sequences have homology to the T46070 GenBank entry described as hypothetical protein T18N14.120 from *Arabidopsis thaliana*, homology to the tomato CF-2 disease resistance genes encoding leucine-rich repeat proteins, and to the tomato CF-9 gene for resistance to *Cladosporium fulvus*. See Table 1 of the subject U.S. patent application as filed.

Applicants respectfully submit that when the Patent Office takes into account the nature and the degree of the homology between the claimed polypeptides and known disease resistance polypeptides as required in the Interim Examination Guidelines, it is clear that the assignment of function as recited in the present claims is based on a "reasonable correlation" between the homologies of the various proteins.

Additionally, SEQ ID NO:13 (Figure 7) teaches the utility of marker assisted selection. The underline sequence TTGAGGGGAAAAGAT teaches the position of a primer that can be extended to score a SNP (C/A change). Section XVI and Table 3 of the subject U.S. patent application show use of a linked marker for this utility. Also, SEQ ID NOs:13 and 14 (Figure 7) show an entire coding region for the protein encoded by the gene found in soybean roots.

Further, Weed Technology: 2000 Vol. 14, No. 1, pp. 156–160 teaches that "Purple deadnettle (*Lamium purpureum*), henbit (*Lamium amplexicaule*), field pennycress (*Thlaspi arvense*), shepherd's-purse (*Capsella bursa-pastoris*)" can serve as hosts for *H. glycines*. "SCN has a relatively broad host range, but its only major agronomic host crop is soybean. Riggs, R.D. 1992. Host range. In R. D. Riggs and J. A. Wrather, eds. Biology and Management of the Soybean Cyst Nematode. St. Paul, MN: American Phytopathological Society. pp. 107–114, reviewed published studies of alternative SCN hosts and compiled a list of 96 genera of Fabaceae (Leguminosae) and 50 genera representing 22 families of

non-legumes that have been reported as alternate hosts of SCN. Most of those studies were conducted prior to 1970 using plant accessions and what is now classified as race 3 SCN from the southern and southeastern U.S. In more recent work, Wong and Tylka (1994) reported that eight common weed species of the U.S. Corn Belt, including Canada thistle [*Cirsium arvense* (L.) Scop.], common cocklebur (*Xanthium strumarium* L.), eastern black nightshade (*Solanum ptycanthum* Dunal ex DC.), field bindweed (*Convolvulus arvensis* L.), common lambsquarters (*Chenopodium album* L.), redroot pigweed (*Amaranthus retroflexus* L.), velvetleaf [*Abutilon theophrasti* (L.) Medic.], and common sunflower (*Helianthus annuus* L.), were nonhosts of race 3 SCN in Iowa. Sortland and MacDonald (1987) had reported previously that redroot pigweed and common lambsquarters were nonhosts of race 5 SCN in Minnesota."

It thus respectfully submitted that the presently claimed subject matter has utility in providing resistance to other plant species, particularly in view of Whitham S, McCormick S, and Baker B. *Proc Natl Acad Sci U S A*. 1996 93(16):8776-81, which shows that resistance genes from tobacco can work in tomato.

Given the utility shown for a nucleic acid encoding an rhg1 polypeptide, applicants respectfully submit that claim 11, which in one embodiment recites such a nucleic acid, is directed to patentable subject matter within the meaning of 35 U.S.C. § 101. Applicants further respectfully submit that claim 71, which recites the production of a transgenic plant, also is directed to patentable subject matter. Claims 13-15 and 17-26 and 72-80 depend directly or indirectly from claims 11 and 71, respectfully, and thus are also directed to patentable subject matter. Applicants therefore respectfully request that the rejection under 35 U.S.C. § 101 of claims 11, 13-15, 17-26, and 71-80 be withdrawn.

Response to the Claim Rejections under 35 U.S.C. § 112, First Paragraph

Response to the First Rejection

Claims 11, 13-15, 17-26, and 71-80 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that since the claimed invention is not supported by either a substantial utility or a well established utility, one of skill in

the art would not know how to make and use the claimed invention. After careful consideration of this rejection and the Patent Office's bases for the rejection, applicants respectfully traverse the rejections and submit the following.

With respect to the first contention, it appears that the Patent Office is basing this rejection on the 35 U.S.C. § 101 rejection presented and discussed hereinabove. The Patent Office's attention is directed to that discussion, wherein applicants have fully addressed the utility rejection presented. That discussion is incorporated here by reference.

Additionally, SEQ ID NO:13 (Figure 7) teaches the utility of marker assisted selection. The underline sequence **TTGAGGGAAAAGAT** teaches the position of a primer that can be extended to score a SNP (C/A change). Section XVI and Table 3 of the subject U.S. patent application show use of a linked marker for this utility. Also, SEQ ID NOs:13 and 14 (Figure 7) show an entire coding region for the protein encoded by the gene found in soybean roots.

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L.), velvetleaf [*Abutilon theophrasti* (L.) Medic.], and common sunflower (*Helianthus annuus* L.), were nonhosts of race 3 SCN in Iowa. Sortland and MacDonald (1987) had reported previously that redroot pigweed and common lambsquarters were nonhosts of race 5 SCN in Minnesota.”

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Furthermore, applicants respectfully submit that the guidance for identifying and isolating a nucleic acid encoding an SCN/SDS resistance polypeptide is sufficient, contrary to the contentions of the Patent Office on page 7 of the Official Action. Indeed, when taken together, Examples 3 and 4 clearly demonstrate to the skilled artisan the identification and isolation of a nucleic acid encoding an SCN/SDS resistance polypeptide.

In summary, applicants respectfully submit that the instant rejection of claim 11, 13-15, 17-26, and 71-80 has been addressed. Accordingly, applicants respectfully request the withdrawal of the instant rejection.

Response to the Second Rejection

Claims 11, 13-15, 17-26, and 71-80 have also been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. After careful consideration of the rejection and the Patent Office's bases therefore, applicants respectfully traverse the rejection and offer the following.

Applicants respectfully submit that the instant claims are directed, *inter alia*, to isolated and purified nucleic acid molecules encoding a soybean *rhg1* and SDS resistance gene. See Figure 3 of the subject U.S. patent application as filed. The gene is capable of conveying *Heterodera glycines*-infestation resistance or *Fusarium solani*-infection resistance to a non-resistant soybean

germplasm, the gene located within a quantitative trait locus mapping to linkage group G and mapped by genetic markers of SEQ ID NOs:1-6, said gene located along said quantitative trait locus between said markers. Positional cloning methods were used to isolate genomic sequences in the chromosomal regions of Forrest that confers SCN/SDS resistance, as further described in Example 4 in the subject U.S. patent application as filed. Specifically, *rhg1* sequences were derived from BAC clones 21D9 and 73P6 of the Forrest *Bam*HI or *Hind*III BAC libraries. In some embodiments, the gene comprises the nucleotide sequence set forth as SEQ ID NO:13 (Figure 7A-7B of the subject U.S. patent application as filed). BLASTP analysis of the translation of the *rhg1* gene (Figure 7C of the subject U.S. patent application as filed), set forth as SEQ ID:14 shows homology to the T46070 GenBank entry described as hypothetical protein T18N14.120 from *Arabidopsis thaliana* (Figure 7E-7F of the subject U.S. patent application as filed), homology to the rice Xa21 disease resistance gene encoding a leucine-rich repeat protein, and homology to the tomato CF-2 gene for resistance to *Cladosporium fulvus* (Figure 7D of the subject U.S. patent application as filed).

Applicants respectfully submit that the instant claims are directed, *inter alia*, to isolated and purified nucleic acid molecules encoding a soybean *Rhg4* gene. The gene is capable of conveying *Heterodera glycines*-infestation resistance to a non-resistant soybean germplasm, the gene located within a quantitative trait locus mapping to linkage group A2 and mapped by the AFLP markers of SEQ ID NOs:6-12, the gene located along said quantitative trait locus between said markers. Preferably, the gene comprises a nucleotide sequence set forth as any one of SEQ ID NOs:16-19. Genes underlying quantitative traits, or genes with related function, such as disease resistance, are often organized in clusters within the genome (e.g., Staskawicz (1995) *Science* 268:661-667). In the case of SCN/SDS resistance, previous studies by the co-inventors of the present invention have suggested that the resistance trait in Forrest may be caused by four genes in a cluster with two pairs in close linkage or by a two-gene cluster with each gene displaying pleiotropy (Meksem et al., 1999). Thus, genomic DNA isolated and disclosed herein comprise multiple resistance gene

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Thus, in the instant specification, the biomolecule is not described solely by a functional characteristic. Sequence data for the genes themselves is also included. Applicants further respectfully submit that between SEQ ID NO: 13, which corresponds to *Rhg1* and any one of SEQ ID NOs: 16-19, which correspond to *Rhg4*, there is over 98% sequence identity. Applicants submit that one of ordinary skill in the art would recognize that there is a disclosed correlation between the function described and the structure of the sequence.

The Patent Office also previously acknowledged that the specification describes AFLP markers associated with the soybean *Rhg4* gene at linkage group A2 mapped by AFLP markers. Applicants respectfully submit, however, that SEQ ID NOs: 16-19 disclose soybean *Rhg4*. Applicants respectfully submit that given the teachings of the instant specification in conjunction with the soybean *Rhg4* gene sequences explicitly disclosed in SEQ ID NOs: 16-19, it would have been apparent to the ordinary artisan that applicants were in possession of the claimed subject matter.

Accordingly, applicants respectfully submit that the rejection of claims 11, 13-15, 17-26, and 71-80 under 35 U.S.C. § 112, first paragraph, has been addressed. Applicants further submit that the claims are in condition for allowance at this time, and respectfully request a Notice of Allowance to that effect.

Discussion of New Claim

New claim 81 has been added. Support for the amendments can be found throughout the specification as filed, including in Sequence Listing and in the claims. No new matter has been introduced. For the reasons set forth herein above, claim 81 is also believed to in condition for allowance and such action is earnestly solicited.

CONCLUSIONS

As a result of the amendments to the specification and claims and the remarks provided herein, applicants respectfully submit that claims 11, 13-15, 17-26, and 71-81 are in condition for allowance. Applicants respectfully request a Notice of Allowance to that effect. Should there be any minor issues outstanding in this matter, Examiner Kruse is respectfully requested to telephone the undersigned attorney. Early passage of the subject application to issue is earnestly solicited.

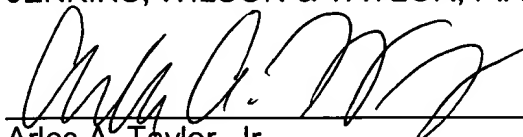
Deposit Account

The Commissioner is hereby authorized to charge any deficiency or credit any overpayment associated with the filing of this correspondence to Deposit Account Number **50-0426**.

Respectfully submitted,

JENKINS, WILSON & TAYLOR, P.A.

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